

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

1. (Currently Amended) A An isolated or purified collagen-binding physiologically active polypeptide having both collagen-binding activity and physiological activity different from fibronectin-activities including collagen-binding activity comprising:

a first peptide having ~~collagen-binding activity and consisting of~~ an amino acid sequence ~~which is identical to an amino acid sequence of protease hydrolysis fragment of fibronectin with at least one protease selected from a group consisting of trypsin, chymotrypsin, thermolysin, plasmin, thrombin, cathepsin D, cathepsin G, pepsin, subtilisin, leukocyte elastase and chymase, and which corresponds to an internal amino acid sequence in collagen-binding domain ranging from 28kDa to 75kDa from the amino-terminal of fibronectin~~ selected from the group consisting of Ala<sup>2</sup> to Trp<sup>341</sup>, Ala<sup>2</sup> to Leu<sup>225</sup>, Ala<sup>2</sup> to Arg<sup>226</sup>, Val<sup>4</sup> to Arg<sup>226</sup>, Val<sup>4</sup> to Trp<sup>341</sup>, Val<sup>119</sup> to Leu<sup>225</sup>, Val<sup>119</sup> to Trp<sup>341</sup>, Leu<sup>225</sup> to Trp<sup>341</sup>, Arg<sup>226</sup> to Trp<sup>341</sup>, Ala<sup>3</sup> to Phe<sup>326</sup>, Ala<sup>3</sup> to Gln<sup>224</sup>, Arg<sup>226</sup> to Phe<sup>326</sup>, Val<sup>4</sup> to Phe<sup>326</sup>, Leu<sup>225</sup> to Phe<sup>326</sup> and Asp<sup>227</sup> to Trp<sup>341</sup> of SEQ ID NO. 1,

fused with

a second peptide having physiological activity different from fibronectin activities including collagen-binding activity.

2. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1 wherein said first peptide consists of an internal amino acid sequence of human fibronectin selected from a group consisting of

~~from Ala<sup>260</sup> to Trp<sup>599</sup> (Ala<sup>2</sup> to Trp<sup>341</sup> of SEQ ID NO.1),~~

~~from Ala<sup>260</sup> to Leu<sup>483</sup> (Ala<sup>2</sup> to Leu<sup>225</sup> of SEQ ID NO.1),~~

~~from Ala<sup>260</sup> to Arg<sup>484</sup> (Ala<sup>2</sup> to Arg<sup>226</sup> of SEQ ID NO.1),~~

~~from Val<sup>262</sup> to Arg<sup>484</sup> (Val<sup>4</sup> to Arg<sup>226</sup> of SEQ ID NO.1),~~

~~from Val<sup>262</sup> to Trp<sup>599</sup> (Val<sup>4</sup> to Trp<sup>341</sup> of SEQ ID NO.1),~~

~~from Val<sup>377</sup> to Leu<sup>483</sup> (Val<sup>119</sup> to Leu<sup>225</sup> of SEQ ID NO.1),~~

~~from Val<sup>377</sup> to Trp<sup>599</sup> (Val<sup>119</sup> to Trp<sup>341</sup> of SEQ ID NO.1),~~

~~from Leu<sup>483</sup> to Trp<sup>599</sup> (Leu<sup>225</sup> to Trp<sup>341</sup> of SEQ ID NO.1),~~

~~from Arg<sup>484</sup> to Trp<sup>599</sup> (Arg<sup>226</sup> to Trp<sup>341</sup> of SEQ ID NO.1),~~

~~from Ala<sup>261</sup> to Phe<sup>584</sup> (Ala<sup>3</sup> to Phe<sup>326</sup> of SEQ ID NO.1),~~

~~from Ala<sup>261</sup> to Gln<sup>482</sup> (Ala<sup>3</sup> to Gln<sup>224</sup> of SEQ ID NO.1),~~

~~from Arg<sup>484</sup> to Phe<sup>584</sup> (Arg<sup>226</sup> to Phe<sup>326</sup> of SEQ ID NO.1),~~

~~from Val<sup>262</sup> to Phe<sup>584</sup> (Val<sup>4</sup> to Phe<sup>326</sup> of SEQ ID NO.1),~~

~~from Leu<sup>483</sup> to Phe<sup>584</sup> (Leu<sup>225</sup> to Phe<sup>326</sup> of SEQ ID NO.1),~~

~~and from Asp<sup>485</sup> to Trp<sup>599</sup> (Asp<sup>227</sup> to Trp<sup>341</sup> of SEQ ID NO.1)~~ corresponds to a

collagen-binding active peptide comprising protease-hydrolysis fragments of human fibronectin with at least one protease selected from the group consisting of trypsin, chymotrypsin, thermolysin, plasmin, pepsin, subtilisin.

3. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1, wherein said ~~protease hydrolysis is a proteolysis~~

~~with a combination of chymotrypsin and plasmin~~ first peptide has an amino acid sequence from Ala<sup>2</sup> to Trp<sup>341</sup> of SEQ ID NO.1.

4. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 3, wherein the said first peptide ~~consists of an amino acid sequence of human fibronectin Ala<sup>260</sup> to Trp<sup>599</sup> (Ala<sup>2</sup> to Trp<sup>341</sup> of SEQ ID NO.1)~~ corresponds to a protease-hydrolysis fragment of fibronectin with a combination of chymotrypsin and plasmin.

5. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1, wherein ~~said protease hydrolysis is a proteolysis with trypsin~~ the first peptide has an amino acid sequence from Ala<sup>2</sup> to Arg<sup>226</sup> of SEQ ID NO.1.

6. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 5, wherein the said first peptide ~~consists an amino acid sequence Ala<sup>260</sup> to Arg<sup>484</sup> (Ala<sup>2</sup> to Arg<sup>226</sup> of SEQ ID NO.1)~~ corresponds to a protease-hydrolysis fragment of fibronectin with trypsin.

7. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1, wherein ~~said protease hydrolysis is a proteolysis with a combination of trypsin and chymotrypsin~~ the first peptide has an amino acid sequence from Asp<sup>227</sup> to Trp<sup>341</sup> of SEQ ID NO.1.

8. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 7<sub>1</sub> wherein the said first peptide ~~consists of an amino acid sequence Asp<sup>485</sup> to Trp<sup>599</sup> (Asp<sup>227</sup> to Trp<sup>341</sup> of SEQ ID NO.1)~~ corresponds a protease-hydrolysis fragment of fibronectin with a combination of trypsin and chymotrypsin.

9. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1<sub>1</sub> wherein said second peptide is a physiologically active peptide selected from a group consisting of a cytokine, insulin, parathyroid hormone and matrix metalloproteinases (MMPs).

10. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1<sub>1</sub> wherein said second peptide is a cytokine.

11. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 10<sub>1</sub> wherein said cytokine is a growth factor.

12. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1<sub>1</sub> wherein said second peptide is fused on the carboxyl terminal side of said first peptide.

13. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 12<sub>1</sub> wherein an amino acid spacer having less than 7 residues is inserted at the fusion site of the first peptide.

14. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 13, wherein a carboxyl terminal of said amino acid spacer is a proteolytic site.

15. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1, wherein said collagen-binding activity is inhibited competitively by plasma fibronectin such that the polypeptide is released from collagen when it is exposed to plasma, serum, or blood, or in the co-presence or upon addition of plasma, serum, or blood, while the polypeptide is retained in collagen in scarcity of plasma, serum, or blood.

16. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1, wherein said polypeptide is produced in bacteria.

17. (Currently Amended) A The collagen-binding physiologically active polypeptide according to claim 1, wherein said polypeptide is produced in a transformant containing a recombinant vector including the gene coding for said collagen-binding physiologically active polypeptide.

18. (Currently Amended) An agent A method for enabling topical retention or sustained release of a physiologically active peptide or a for physiological activity-imparting agent ~~which contains~~ using the collagen-binding physiologically active polypeptide of claim 1, wherein the collagen-binding physiologically active

polypeptide after binding to collagen exhibits physiological activity thereof at or near the site of administration either by being retained by the collagen or by being gradually released from the collagen.

19. (Original) A biomaterial comprising a composite wherein the collagen-binding physiologically active polypeptide of claim 1 is combined with collagen or gelatin.

20. (Currently Amended) ~~An agent~~ A method for enabling topical retention or sustained release of a physiologically active peptide or a for physiological activity-imparting agent ~~which contains~~ using the biomaterial of claim 19, wherein the collagen-binding physiologically active polypeptide after binding to collagen exhibits physiological activity at or near the site of administration thereof either by being retained by the collagen in or by being gradually released from the collagen.